

Master of Science Thesis

Developing Clinical Trials in The Portuguese Family Medicine

Challenges and Opportunities in the European Context

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Acronyms and Abbreviations

ACES – Agrupamento de Centros de Saúde (En: Group of Health Centres)

ACSS – Administração Central do Sistema de Saúde

AMPIF – Associação de Médicos Portugueses da Indústria Farmacêutica

APIFARMA – Associação Portuguesa da Indústria Farmacêutica (En: Portuguese Association of the Farmaceutical Industry)

ARS – Administração Regional de Saúde (En: Regional Health Administration)

BRIC – Brazil, Russia, India and China

CEIC – Comissão de Ética para a Investigação Clínica (En: Ethics Committee for Clinical Research)

CNPD – Comissão Nacional de Protecção de Dados (En: Data Protection National Commission)

CPVO – Community Plant Variety Office

EAHC – Executive Agency for Health and Consumers

ECRIN – European Clinical Research Infrastructures Network

ECDC – European Centre for Disease Prevention and Control

ECHA – European Chemicals Agency

EEA – European Environment Agency

EFSA – European Food Safety Authority

ENSP – Escola Nacional de Saúde Pública

EGPRN – European General Practice Research Network

EIT – European Institute of Innovation and Technology

EMA – European Medicines Agency

EMCDDA – European Monitoring Centre for Drugs and Drug Addiction

ERC – European Research Council

ETF – European Training Foundation

EURACT – European Academy of Teachers of General Practice / Family Medicine

EUROFOUND - European Foundation for the Improvement of Living and Working Conditions

FCT – Fundação para a Ciência e Tecnologia

FMUL – Faculdade de Medicina da Universidade de Lisboa

GSK – Glaxo Smith Kline

HPV – Human Papiloma Virus

INFARMED – Autoridade Nacional do Medicamento e Produtos de Saúde (En: Portuguese National Authority for Drugs and Health Products)

PNEC – Plataforma Nacional de Ensaaios Clínicos (En: National Platform for Clinical Trials)

PtCRIN - Portuguese Academic Clinical Trials Infrastructures Network

PwC – PricewaterhouseCoopers Portugal

REA – Research Executive Agency

RPCG – Revista Portuguesa de Clínica Geral (Currently RPMGF; En: Portuguese Journal of General Practice)

RPMGF – Revista Portuguesa de Medicina Geral e Familiar (Former RPCG; En: Portuguese Journal of Family Medicine)

UCSP – Unidade de Cuidados de Saúde Personalizados (En: Personalized Health Care Unit)

UKCRN – United Kingdom Clinical Research Network

USF – Unidade de Saúde Familiar (En: Family Health Unit)

WONCA – World Organization of National Colleges, Academies and Academic Associations of General Practitioners / Family Physicians

Keywords

Clinical Trials; Europe; Family Medicine; General Practice; Portugal.

Abstract

Introduction: The hypothesis of this thesis is that there could be a much greater number of Clinical Trials in Portuguese Family Medicine if obstacles were removed and opportunities explored properly.

Background: In Portugal there is a new generation of Family Doctors that is assuming permanent positions all over the country and is accepted to be the most well prepared generation ever.

Methods: Search on MEDLINE. Relevant articles were also identified in the only journal dedicated to Portuguese Family Medicine, RPMGF. A search was made on Portuguese health policy textbooks and national health plan policy. INFARMED was also contacted and their reports about Clinical Trials were analysed. Portuguese Family Doctors themselves were contacted and invited to answer questionnaires. Besides that, fifteen key opinion leaders related to Portuguese Medicine were approached for solutions.

Results: According to INFARMED data, from 2006 to 2011 there were only four health centres involved in clinical trials. In Portugal there is: A negligible number of academic trials; almost no support infrastructures or training; inefficiently used electronic health records; a research weakly linked to medical careers; an uninformed isolation internally and externally; an already complex European Union regulation that is compounded even more; Scarce funding for clinical research. Portuguese Family Doctors are keen to actively participate in a change.

Discussion: With the present results the diagnosis for the current situation is clearly negative. Fortunately there are very good opportunities to improve.

Conclusion/Recommendations: Time, money and support must be given to Portuguese Family Doctors. In this context, twenty recommendations are provided intending to promote a true change in Portuguese Family Medicine Clinical Trials panorama.

Keywords: Clinical Trials; Europe; Family Medicine; General Practice; Portugal.

Resumo

Introdução: A hipótese colocada nesta tese é a de que poderia haver um número bastante mais elevado de ensaios clínicos na medicina familiar portuguesa se os obstáculos fossem removidos e as oportunidades exploradas de modo adequado.

Contexto: Em Portugal existe uma nova geração de Médicos de Família que está a assumir postos de trabalho um pouco por todo o país e que é aceite como sendo a mais bem preparada geração de sempre.

Métodos: Busca na MEDLINE. Leitura de artigos na única publicação científica dedicada à Medicina Geral e Familiar – RPMGF. Consulta em livros portugueses de política da saúde e acerca do Plano Nacional de Saúde. O INFARMED foi contactado e relatórios seus sobre ensaios clínicos foram analisados. Os Médicos de Família portugueses foram contactados e convidados a responder a questionários. Além disso, quinze personalidades da Medicina Portuguesa foram chamadas a sugerir soluções.

Resultados: De acordo com dados do INFARMED, de 2006 a 2011 houve apenas quatro centros de saúde envolvidos em ensaios clínicos. Em Portugal: Existe um número pouco significativo de ensaios académicos; Praticamente não há infraestruturas de suporte ou treino; Os registos clínicos eletrónicos são usados de forma ineficiente; a investigação é fracamente ligada às carreiras médicas; há isolamento interno e externo; a já complexa regulamentação da União Europeia é complicada ainda mais; há um subfinanciamento da Investigação Clínica. Os Médicos de Família portugueses estão disponíveis para participar ativamente numa mudança.

Discussão: Com os presentes resultados o diagnóstico para a presente situação é claramente negativo. Felizmente existem muito boas oportunidades para melhorar.

Conclusão/Recomendações: Tempo, dinheiro e apoio têm de ser fornecidos aos Médicos de Família portugueses. É nesse sentido que são fornecidas vinte recomendações para obter uma verdadeira mudança no panorama dos Ensaios Clínicos na Medicina Familiar portuguesa.

Palavras-Chave: Ensaios Clínicos; Europa; Medicina Familiar; Clínica Geral; Portugal.

1. Introduction: Hypothesis and the Need to Explore It

The hypothesis of this thesis is that there could be a much greater number of clinical trials in Portuguese family medicine if obstacles were removed and opportunities explored properly. This work started with the belief that the confirmation of this hypothesis through sound methodology can lead to a set of implementable recommendations to increase the number and quality of clinical trials in family medicine in Portugal.

Family medicine is a scientific discipline recognized worldwide, where clinical practice, education and research should walk hand in hand for the benefit of patients. In Portugal it has advanced slowly but surely. First it conquered its space in clinical practice. Secondly it is establishing educational departments in medical schools. Thirdly it must increase its clinical research. It is in research that it significantly lacks behind other countries' family medicine. Research is crucial because if any scientific discipline ignores it then it is condemned to stagnation and deterioration. Therefore, it is in family medicine best interest to advance clinical research.

Within the need to advance clinical research this thesis is focused specifically on clinical trials. This is because such trials are the most complex type of research and if they become routine, then the whole clinical research universe in family medicine will be improved.

It is important to increase clinical trials across Portuguese medicine and it is also important to do research in primary care, so that it complements that done in hospitals.

When studying a drug already in the market, with an ambulatory indication and with characteristics for primary care patients, there is not an excuse for not testing it in a family medicine setting. There are plenty of good and relevant research topics for family medicine. The true effectiveness of an innovation can only be judged in appropriately designed clinical trials conducted in the setting where the innovation will be applied. (Peterson, 2006) That is unquestionable. Research done in hospitals cannot always appropriately represent the community patients in which the drug will be used often and chronically.

In order to develop Portugal's Health Care System, there is a need to enhance the research capacity and to engage family doctors in clinical research. Only this option will promote the right questions to be asked, evaluating patient oriented outcomes. If research

becomes abundant then health outcomes will be studied and family medicine itself, as a technical and scientific discipline, will be significantly improved in the country.

In the real world, real primary care patients have co morbidities, but most of the guidelines, have been developed based on studies ignoring co morbidities. (W. Beasley, Starfield, van Weel, W. Rosser, & L. Haq, 2007) This knowledge is an opportunity to develop clinical research in primary care settings with real world patients. While compliance is not considered as an outcome, researchers in primary care should also bear in mind that a lack of compliance in the “real world” frequently renders an efficacious intervention ineffective, and they should address this issue in their study design. This will usually involve consideration of additional social and emotional endpoints. (Lionis C, 2012) Family medicine research, with its focus on the person’s health and effective delivery of care, has a key role to play in bridging the gap between the laboratory and practice. (L. K. Lam, 2004) It is the only discipline which can do it spontaneously. With its holistic approach to medicine, family medicine approaches to patients with all their complexity of biologic, psychological and social factors. It deals with the real people in a real context – their communities – with all the co morbidities a doctor must deal with, including confounding factors that were never thought about previously by scientists far from the clinical setting and, by definition, with difficulties to identify problems in the passage from the bench to the patients’ bedside. The age of family medicine research will come when all medical research will require the input from family medicine to assure its validity, relevance, applicability, and generalizability. (L. K. Lam, 2004)

How can Portuguese family medicine take the next steps in order to advance and achieve better results in clinical research? To answer that question, the low performing (in terms of clinical research) Portuguese primary care and other more prolific European primary care settings were analysed. Primary care clinical research in other European countries is flourishing. For example in England, networks are established and many doctors assume as part of their professional life that clinical research in general, and particularly clinical trials, do have interest. It is common to see stated clinical research activity interest when job vacancies are advertised for a GP practice.

In 2014 there is a dearth of clinical trials in Portuguese family medicine. Clinical trials are almost inexistent. The few that have obtained regulatory approval (which does not mean that they were even able to recruit patients) were all sponsored by the pharmaceutical industry. Industry sponsored trials are well funded and provide the doctor investigator with guidance and resources from the company. Their weakness is that is mainly profit oriented so if the molecule patent has expired or, alternatively, if it is for few patients, then it will not be done. Investigator initiated (academic) trials complement such research by exploring questions that the industry does not want to, or has no interest in answering. They have scarcer funding available and demand much more from the doctor who will have to design the protocol alone and deal with the overwhelming requirements. Both types of trials are useful and at least in the beginning, it would be very useful if at least industry trials could flourish and, around them, infrastructures which would enable academic trials. However, family doctors cannot delegate research only in pharmaceutical companies. Family doctors cannot ignore research useful for patients just because they do not have, economically speaking, a commercially “interesting” problem for the industry.

Other than the obvious dearth of trials, the background of clinical trials in Portuguese family medicine is almost inexistent. That is precisely why this thesis will, in the results section,

deliver an overview of family medicine trials by enquiry and review of the scarce material available. That is an important contribution of the present work. Only if the problem is fully uncovered and explored can a solution begin to be constructed based on removing obstacles and exploring the opportunities to increase the trials.

João Lobo Antunes classifies three types of advantages in having Clinical Research:

1. Healthcare – better quality of care with faster access to innovative drugs;
2. Educational and scientific – opportunity for researchers to collaborate with their peers in national and international programs;
3. Economic – more jobs in research and development, acquiring new competences.

In fact, these are inseparable and improve each other in an endless spiral. The best of all is the final result – a better society with a stronger economy, with outstanding healthcare quality constantly fed by an exciting ambience of innovation and high standards in research and education.

It is long time known that a strong primary health care system is essential to provide effective and efficient health care. And it is also true that research in primary care is essential to inform practice and to develop better health systems and health policies. (W. Beasley, Starfield, van Weel, W. Rosser, & L. Haq, 2007) A country like Portugal must succeed in bringing family doctors to do clinical trials. The opposite is not even an option. The financial and economic crisis will have an end. Changing the status quo will then be crucial to Portugal affirm itself as a fully developed country with the ambition of becoming a world leader.

Specifically, Clinical Trials have several advantages:

- Keep health units updated on top care;
- Provide new treatment options to patients;
- Generate highly qualified jobs (doctor Investigators supported by research nurses, biostatisticians, database managers, investigational drug pharmacists, clinical monitors, regulatory managers, etc.);
- (Academic ones) help translate into patient benefits from the work of basic researchers;
- (Industry ones) are a significant source of income for countries and institutions clever, competitive and committed enough to attract them.

There is a need to develop Clinical Trials in Portuguese family medicine. Change is the most natural thing in the world. When the current status is not appropriate, the wisest decision is to promote the evolution to something better. Continuous improvement is always recommendable. In order to ensure that clinical research rapidly and successfully advances practice, clinical researchers need to develop new partnerships with primary care providers who deliver the majority of care to the population. These partnerships should enhance the ability of investigators to conduct research, as well as facilitate delivery of better tools to clinicians to provide care. (Peterson, 2006)

2. Background

It is important to develop a national program for research in health. The European scientific panorama in the health field is extremely vast, taking a leading role in the investment in research and development, coordinating the scientific national systems and promoting scientific excellence. (Campos & Simões, 2012) The absence of an effective primary care research infrastructure as it happens in countries like Portugal is impairing the development of local and national healthcare systems that have the potential to bring about dramatic gains in improving the health of the world's populations. (W. Beasley, Starfield, van Weel, W. Rosser, & L. Haq, 2007) Investment must be done. A greatly increased commitment on the part of international organizations both within and outside of primary care is needed. (W. Beasley, Starfield, van Weel, W. Rosser, & L. Haq, 2007) Family doctors need time and infrastructures to develop clinical trials. That will be the only way to get answers to the questions that arise in family medicine context. In the future, eventually, the production of more high-quality work will gain the trust from editors. (L. K. Lam, 2004)

Following there is a synopsis of Portuguese family medicine, focusing on relevant constraints and boundaries of this discipline, to help us understand how clinical trials can or cannot flourish within this specific environment.

2.1 Worldwide Principles of Family Medicine

Family Medicine, as stated by Ian R. McWhinney in his “A Textbook of Family Medicine”, is a body of knowledge characterized by a system of values and an approach to problems – that is identifiably different from that of other disciplines. In this same book he describes nine principles for this medical discipline:

1. Commitment with the person rather than to a particular body of knowledge, group of diseases, or special technique;
2. The ambition to understand the context of the illness;
3. Every contact is an opportunity for prevention or health education;
4. Single patients versus population groups – both must be addressed;
5. The doctor as part of a community wide network of supportive and health care agencies;
6. Ideally, doctors and patients would share the same habitat;
7. Seeing patients in their homes is part of the job. Knowing the home give us a tacit understanding of the context or ecology of illness;

8. The importance of the subjective aspects of medicine. Doctor must be sensitive to feelings and have an insight into relationships;
9. The doctor as a manager of resources.

These nine principles are generally accepted to characterize Portuguese family medicine as well.

2.2 Family Medicine in Portugal

In Portugal this discipline started with non-specialist doctors but progressively evolved into something more. Currently it has a five year internship program (one general year common to all the other medical internships plus four vocational training years).

Medical schools progressively created family medicine departments and the discipline itself is slowly conquering space in the medical courses *curricula*. Critical mass is being gained and highly respected strong personalities have arisen and can debate on equal foot with colleagues from other specialities.

In the public sector, Portugal, as many other European countries, currently has its National Health Service divided in different levels of care:

- Primary Care – where family medicine and public health is developed;
- Secondary Care – hospital medical specialties;
- Tertiary Care - where specific reference centres have its place as a last available resource.

In family medicine clinical practice, the individual and family life cycle is fully covered, and as long as highly trained doctors assume their role, its quality is visibly growing every day.

Unfortunately, family medicine still has an important handicap. Since politicians and the population generally ignore the need for specialized doctors in this field, it is still frequent to see non-specialized doctors practicing family medicine.

The new generation of family doctors that is assuming permanent positions all over Portugal is accepted to be the most well prepared generation ever. Unfortunately there is a generalized doubt about the capacity of the country and its National Health Service to reap all the benefits it could from such qualified doctors. Underpaid, not fully recognized as a valuable human resource and deeply submerged in bureaucracy, these doctors tend to be pessimistic about their future and aren't sufficiently stimulated to develop and assume as their own, techniques and many other skills that in some countries are considered an advantage and a stimulus to the daily clinical practice.

According with ACSS data, in 2007, 71% of the health centre's doctors were above 50 years old and only 9 percent had less than 35 years old. (Carmo, 2012) It is important to describe the current status of the public primary care network. The truth is that primary health care does not have grown in the proportion of the needs. (Carmo, 2012)

In the last years, there was a reform for this level of care, transforming some of the health centres in units oriented for objective accomplishment and pay for performance. This reform now, with the financial incapacity of the public budget (related with the economic crisis), is much slower than in the beginning and professionals feel that the network will probably be at least partially privatized - something that is not giving convincing results in other countries.

In the current primary care public context, there are two different models for working in family medicine: UCSP (Unidades de Cuidados de Saúde Personalizados – En: Personalized Health Care Units) – the ones that work with no financial incentive and that employ the doctors who don't want to work in a pay for performance model - and USF (Unidades de Saúde Familiar – En: Family Health Units) – the (at least in a more mature phase) pay for performance model.

USF were created from voluntary candidatures from groups of doctors and other professional teams. They distinguish themselves, in the essential, from the UCSP, for the fact of having origin in a voluntary adhesion, having mandatorily an information system and, in a late phase, its remuneration regime being based in the professional development and incentives, and having a model of contracting and performance assessment. (Boquinhas, 2012)

There are three types of USF models: A, B or C. The difference between the models results of the degree of organisational autonomy, the retributive model differentiation and incentives for the professionals, and the financial model and respective legal status. Model A is the less differentiated from the organisational point of view, corresponding to a kind of learning and improvement of the team work and on the first steps in techniques of contracting. Model B is the most suitable for teams with a greater degree of maturity and organisational development, also with greater requirement in the matter of contracting. Model C is intended to be a real contract program with clear objectives and a large degree of requirement in compliance. (Boquinhas, 2012)

The population enrolled in each USF cannot be inferior to 4000 neither superior to 18000. In the beginning of 2012 there were active in the “continental” Portugal 315 USF, from which 168 model A and 147 model B. Accepted for assessment, there were more 387 candidatures that were waiting for an eventual order of approval. (Boquinhas, 2012)

Even though it does attract many family doctors, the pay for performance model has weaknesses. Probably the most severe is that financial incentives come from general statistic process indicators, far from measuring the quality of the medical practice and, at times, even diverting professionals from the principles of family medicine. The clinical practice becomes more automatic and reduced to the accomplishment of some statistic objectives. This may ignore the patient itself and reduces the human touch and “art” in medicine.

In UCSP it is important to refer that despite being a more conventional model of care, it still exists rigor in how they should work, especially as regards to the offer of a basic portfolio of services, hours of operation, well defined system of providing care and guidance of users, prescription renewal system, professional replacement system, liaison with other functional units of the ACES (Agrupamento de Centros de Saúde – En: Group of Health Centres), and a possible additional services portfolio. (Boquinhas, 2012)

Common to UCSP and USF models, there is a great general weakness– the pressure to see patients in a short period of time. While it is true that this pressure is useful to increase the number of patients that have access to a family doctor when one is needed, it is also true

that the very usual Portuguese 15 minutes available for each consultation are not enough to satisfy all the patients' needs. Some can say that in other countries the consultations are even shorter, but in those same countries, patients' needs aren't also totally satisfied.

In the current days, a whole generation of family physicians over 50 years old is literally thinking about retirement. They are burned out and totally tired of bureaucracy that should have been delegated a long time ago to support personnel. The country does not need doctors dealing with bureaucracy. It's a complete waste of money and highly qualified people. People with so much potential are the richness of a country. How can Portugal waste it like that? Stimulus is what this fine class of people need. Stimulus to take the best they are able to give. Who would not become burned out when with so much intellectual capacity sees nobody expects more from him than taking care of bureaucracy? Lately, Portuguese nurses have been asking to assume medical functions. They do not understand the real issue. It's bureaucracy that doctors really need to delegate. That's what doctors must delegate as soon as possible. Doctors need real clinical secretaries, trained for dealing with bureaucracy, letting for them the highly complex work for what they were trained for.

In the private sector problems are different. There are the family doctors who work on their own as partners, and the ones who work for private larger institutions, as salaried family doctors. In either case, team work and continuous medical education tend to be forgotten. There's also the problem of existing usually as non-organized and not-well defined units specifically for family medicine. It is common to include doctors trained in internal medicine or simply not specialized at all. Family medicine should be done by doctors specifically trained in family medicine.

A good advantage of the private sector is the possibility of working with less time pressure (more flexibility to increase the quality, please and attract the patient), which can help in the doctor-patient relationship.

Finally, in both public and private sectors, there is a common problem of communication between professionals. Notes in medical records tend to be scarce and unlinked; communication between several doctors from different areas and who serve the same patient is absent most of the time.

3. Methods

The original search regarding the status of Portuguese clinical trials, its obstacles and opportunities comprised the electronic bibliographic international database MEDLINE. The keywords were: Clinical Trials; Europe; Family Medicine; General Practice; Portugal. Relevant papers, with same keywords but in Portuguese were also indentified in the only journal dedicated to Portuguese Family Medicine - RPMGF (previously titled RPCG). Due to the scarcity of either international or national articles found about this topic, a search was made on Portuguese health policy textbooks and national health plan policy documents looking for any material relevant to trials in family medicine. Mass Media were also consulted. The regulatory agency responsible for the approval of such trials, INFARMED, was also contacted and their reports about clinical trials were analysed. At the end, this thorough search produced very limited secondary and tertiary information (because such information is indeed scarce even at European level). Therefore, it was necessary to talk with the actual protagonists of family medicine clinical trials in Portugal. The family doctors themselves were asked to answer to questionnaires. Three questionnaires gathering new data shared on this thesis were submitted to web (email) based discussion groups composed of family doctors (and family medicine trainees), i.e. MGF XXI, MGFamiliar, MGFClínica and EURACT-PT, and using the social network Facebook. The few family doctors who actually have conducted clinical trials in Portugal were approached. Besides, fifteen Key Opinion Leaders were questioned about ways of developing Clinical Trials in Portuguese family medicine.

4. Results

4.1 Literature Review and Interviews on Family Medicine Clinical Research

In 2007, a report prepared by OECD about the assessment of Higher Education in Portugal and the strategic government document “Compromisso com a Ciência” marked the beginning of a remarkable evolution of the scientific Portuguese system. This is put in evidence as an increase in the following indicators:

- Number of active researchers;
- Number of graduates in mathematics, sciences and technology;
- Number of new doctorates;
- Public and private investment in research and development;
- Number of international scientific papers;
- New patent submissions.

Besides the favourable evolution of these indicators, important university legal regime reforms were done promoting the internationalization of the Portuguese scientific system by establishing agreements for partnership with global reference institutions. (Campos & Simões, 2012)

Research in the health area has currently the following funding options:

- Public – fundamentally by the Ministry of Science and Technology through FCT (Fundação para a Ciência e Tecnologia);
- Foundations – usually with their own agenda (Fundação Gulbenkian, Fundação Champallimaud, Fundação Francisco José dos Santos, Fundação Bial);
- Pharmaceutical Industry, including Contract Research Organizations.
- International Funding – particularly through the European Union funds;
- Patronage – unfortunately far from as common as in USA or UK;
- Personal or own institution funding – not probable in the current context. A possible alternative is to contract research with appropriate incentives;
- Scientific Societies – many times with pharmaceutical funds; such funding rarely seeks to encourage new projects or groups. (Antunes, 2010)

An important note is that most of these favourable indicators and the majority of the science funding in the health arena go to basic research (i.e. at molecular level) or animal (pre-clinical) research, rather than clinical research.

In Portugal, until 2004, there was no national ethics committee. Its creation, (the national ethics committee is named CEIC) in that year was an important step to enable Clinical Trials nationwide. However, for a while although there was a national ethics committee there were no local ethics committees specifically for primary care, e.g. in ARS (Administração Regional de Saúde - Regional Health Administration), like there were in hospitals.

According to INFARMED data, from 2006 to 2011 there were only four health centres involved in clinical trials: Lapa (2 trials), Eiras (1 trial), USF Briososa (1 trial), and USF Santo André de Canidelo (1 trial). This is a meagre and dramatic reality where nationwide clinical trials in primary care can be counted using hands. Following are two examples of these rare units where clinical trials were performed.

4.1.1 Comprehensive Clinical Trials Report by PwC

In June 2013, PricewaterHouse Coopers (PwC) presented a report asked by APIFARMA entitled “Ensaaios Clínicos em Portugal” (En: “Clinical Trials in Portugal”). While this report was not specifically focused on the Family Medicine setting, given the detailed description and analysis of the Portuguese context in regards to clinical trials, it was considered necessary to present some interesting data that the report describes.

This report confirms the dramatic decrease in the number of clinical trials that were submitted in Portugal between 2006 and 2012 – 26% decrease (from 160 trials to 118 trials). The historical minimum since 2006 was achieved in 2011 with just 88 trials. The rate of clinical trials per one million inhabitants is one of the lower ones in Western Europe.

As recommendations, PwC report highlights the following as some of the most significant:

- Modification of the current legislation in order to reduce the timings between submission of trial proposal and the actual beginning of the subject recruitment – something considering highly limitative for clinical trials in Portugal;
- Training of clinical trial centres for conducting the activity, namely through the creation of dedicated structures and by promotion of a larger integration and cooperation between stakeholders;
- Creation of adequate incentives to promote the involvement of researchers and other professionals in clinical trials.

This study presented in June 2013, also concluded that for each €1.00 invested in clinical trials there is €1.98 return for the Portuguese economy. The problem is that return is not being availed. In fact, as it was mentioned by João Almeida Lopes (APIFARMA President) in 2012, the pharmaceutical companies’ investment for Clinical Trials in Portugal was calculated

in 36 million Euros. That, by itself, contributed for savings of 3.5 million Euros on the public expenditure related with medication and exams. (Diário Económico, 2014)

But the problem with Clinical Trials is not just related with Portuguese Family Medicine. As João Almeida Lopes (APIFARMA President) says, Portuguese Clinical Trials as a whole would be improved if there was a review on the legislation that allowed a reduction of the timings between clinical trials' submission for approval and the actual recruitment start. (Diário Económico, 2014)

4.1.2 The Decline of the “Doctor-Scientist”

As João Lobo Antunes states in his “Investigação Científica e Plano Nacional de Saúde” (2010, En: “Scientific Research and the National Health Plan”), one of the problems about research in Portugal is related with the decline of the “doctor-scientist” which is seen since at least the 1980's.

This issue is a true obstacle felt everyday by any doctor and this is especially seen in the family medicine setting. The clinical work has *swallowed* the scientific work. Without the last one, will the doctor maintain his characteristics? What happened to the “doctor-scientist”? Why this happened?

According to João Lobo Antunes, this happened because:

1. Current faster scientific progress compared to the past makes it harder to a doctor who wants to dedicate himself simultaneously to research and clinical work;
2. Demanding management models, combined with doctors scarcity and high clinical goals, turn it difficult to make both clinical and research work;
3. There's a medical education with insufficient focus in the scientific component and an internship that tends to be long and not to value research, associated with the absence of role models in the clinical units – progressively faraway from the academic world;
4. There's a weak academic reward. This is specifically visible when realizing the fact that teaching and research have a too small importance in the medical careers progression.
5. It is difficult to obtain financing, for example, because basic research projects tend to be more competitive;
6. Does not exist support units to research, namely for clinical trials execution, bio statistical support or electronic medical notes / databases;
7. There's a complete absence of research priority in the strategy of the Health Units.

The decline of the “doctor-scientist” is tragic for Medicine. It is our responsibility to invert it and bring medicine to its own place. Society needs doctors linked to the highest scientific standards. The new generation must create a new model for practicing medicine and become new role-models for the future generations. People like our last Medicine Nobel Prize Egas Moniz are needed. Portuguese medical schools need them and actually are able to generate new “doctor-scientists”.

Western medicine was not always as scientific as currently. Even in the beginning of the 20th Century, myths and beliefs were not totally eradicated. Empirical approaches were not unusual and the evolution was slow. Things have changed and an intense effort is being done in order to advance research.

A long way is still ahead. The truth is, many drugs currently approved are not scientifically supported for the way they are used (e.g. off label) and even so, they can be authentic “best-seller” drugs. The only explanation for this fact must be that doctors still are not as scientific in their approach to patients’ treatment as they should. Pharmaceutical industry marketing probably is involved on it. It “sells” catchy sentences that appeal to the empirical and the non-scientific approach to patients’ treatment. The inattentive doctors, not savvy on research, can easily be manipulated and become almost as puppets in the pharmaceutical industry hands. That, for sure, will not be good for the communities and patients.

To counter this problem, movements like the ones associated with evidence-based medicine and rational prescription are spreading a message of scepticism and rational analysis of the science behind the clinical work. Evidence-based medicine must take the place of “eminence-based medicine” or simply “faith-based medicine”.

A way to improve family medicine is to make it as scientific as possible, moving it away from the myths and beliefs that have a capacity to resist by habit and persist even with nothing tangible to support it.

Doctors must be educated as researchers since their most basic education, as *non-believers*. Believing is *enemy* of science. Scepticism is the key. In a scientific world, the mind must be open to doubt and to question everything. No dogmas are allowed. The answer must be found through the old well known scientific method. That’s where research, and specifically clinical research, enters and has one of the main roles.

There are many modalities to do clinical research: observational, experimental, transectional, longitudinal... Researchers are plenty of options to work on. It all depends on the question you are dealing with.

It’s true that it’s not with a single study that you can assure anything but, if the result comes over and over every time you test the hypothesis, the odds of being right get bigger. It’s the repetition of the same phenomenon over and over that makes it plausible through the scientific method and that’s when evidence-based medicine comes with its metanalysis giving us even stronger evidence by stratifying the current state of the knowledge on a certain theme and offering new and fresh research questions.

It’s in this ambient that ideally a country would like its doctors to be grown up. In it, patients are better assessed and treated. With a *scientific medicine* it is guaranteed that life expectancy and even more important, the quality of life, will grow. And the good news is that this pays for itself. With a scientific approach, superfluous treatments are eradicated and secondary effects resulting from useless drugs are prevented. This is, in fact, the basis for quaternary prevention concept – the prevention of iatrogenesis.

What if we think about economy? What can a country gain with a more scientific family medicine? Besides a more active population, the country can also be able to create drugs and other devices that can then be commercialized with others and be a fountain of wealth. A stronger economy will arise. Even if it never develops a new drug, a country that

invests in clinical trials will attract pharmaceutical industry funds and create highly qualified jobs.

General practice/family medicine research is also necessary to increase the attractiveness of general practice/family medicine to medical students and graduates. (Hummers-Pradier E. e., 2009) In times when Portuguese family medicine is so constrained when it comes to human resources, this must be taken in account.

What about patients' satisfaction? Helping other patients throughout the world will be a reason for satisfaction. If not for such an altruist reason, patients' satisfaction will arise from the fact that their being seen by *top doctors* who do research and presumably are aware of the better options for solving their specific problems. Patients will also know that, if needed, they will have the opportunity to test new more advanced therapies in a secure and controlled environment.

The 21st century should be a golden age of family medicine research because the time is right for our discipline, the health care environment is most suitable, and stakeholders are supportive. (L. K. Lam, 2004) Research in the Portuguese primary health care must be at the forefront of innovation. We need to think globally, instead of investing only in local studies, it is necessary to seek and establish the right partnerships and find the necessary funds and infrastructures. (Braga, 2011) The return of the *doctor-scientist* is a priority. It would not be reasonable to waste an intellectual elite like Portuguese family doctors. A country like Portugal cannot afford that.

4.1.3 Subjects recruited in Primary Care Settings

When recruiting subjects, the investigator have to take into account that many times, in primary care settings, patients suffer from less severe clinical conditions and are more heterogeneous both in demographic and in clinical characteristics when compared with patients recruited in secondary care settings. They may have a lower probability of disease, or the disease may be diagnosed at a less severe stage, and they often report undifferentiated symptoms. Thus, restrictive selection criteria may result in limited applicability of the trial in primary care. (Lionis C, 2012) Armando Brito de Sá confirmed that this was one big problem in a clinical trial he was involved in still in the 1990's at Centro de Saúde de Sete Rios. While this heterogeneity can be problematic for phases II, III or IV, where criteria selection must take into account these facts, it is also true that healthy patients ideally and usually do not recur to the secondary care. So we can admit the characteristics of primary care patients can be both a challenge and an opportunity. Family physicians must know how to best deal with it and make it always an advantage. The design of a randomized clinical trial in primary care should explicitly consider diversity in factors such as age range, participants' levels of education, economic status, and multi-morbidity. Exclusion criteria should be kept to a minimum. The fact is - recruiting patients from a variety of primary care settings can assist in creating a valid sample. (Lionis C, 2012) If you keep this in mind, clinical trials will have high quality.

4.1.4 Challenges

The problem with clinical trials in Portugal is not exclusive to family medicine, although it is more severe in this speciality. In fact, it crosses all of the Portuguese medicine. Note figures 1 and 2.

In September 2012 Agência Lusa reported that clinical trials occurring in Portugal were falling since 2008. In 2012, in the first six month there were 53 new clinical trials registered versus 108 in the equal period for 2005. These are total numbers representing all the research areas. It means that if family doctors want to improve clinical trials, they will have to face an adverse setting. However, isn't it true that it is in the hardest times that the best of our characteristics must come to surface and make us surpass the obstacles?

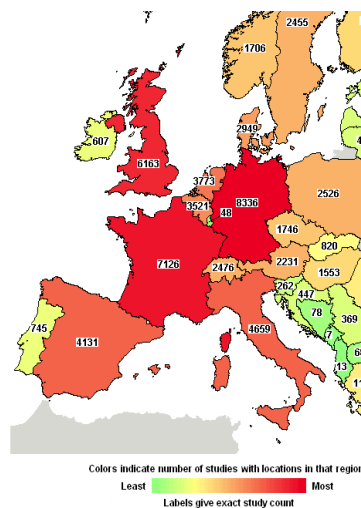


Figure 1 – Map of Clinical Trials in Europe (Source: ClinicalTrials.gov consulted Jan. 2012 for Year 2011)

For Peter Villax, responsible for innovation at Hovione, the main obstacle to clinical research in Portugal is the intervention of the CEIC. With the aim of protecting the health and safety of patients, CEIC have much preferred to err on the side of caution that today there are virtually no clinical trials in Portugal. There is the need for a balance between the desire to protect patients and the need to discover, test and develop innovative new treatments. (Diário Económico, 2014)

The current panorama is not an easier one to overcome. In Portugal, even considering all health field clinical research, there is:

- A negligible number of academic trials;
- Almost no support infrastructures or training;
- Inefficiently used electronic health records;
- A research weakly linked to medical careers;
- An uniformed isolation internally and externally;
- An already complex EU regulation that is compounded even more;

- Scarce funding for clinical research.

Even considering commercial clinical trials, Portuguese numbers are incomparable lower to the ones USA, European Union or BRICs have, already taking in account the dimension factor.

David Silvério Rodrigues, a Family Doctor working at UCSP Torres Vedras (Extensão Silveira) in February 2014 questioned his peers about what was hampering clinical research in Portugal. He obtained 21 answers and concluded that there were basically two distinct types of reasons:

1. Absence of research culture (with no research policies implemented; no specific legal statute for being PhD Student and Senior Doctor; no time for doctors to do research; absence of acknowledgment for the importance of research; no team work; low importance for curricular purposes);
2. Weak or even total absence of resources and funding (with not enough grants available; not appropriate education for research; dearth of clinical research centres; long waiting times for approval for research studies).

Still on the context of the question made by David Silvério Rodrigues, I would like to highlight three different visions from three different Portuguese family doctors: Mónica Granja, Frederico Rosário and Tiago Sousa Veloso. I chose them because from the answers I had access to, its assertiveness was especially striking.

Mónica Granja reported seven reasons contributing for the hampering of Clinical Research in Portugal:

1. Work in ethics committees done within the free/leisure time of its members;
2. Multicentre trials with the need for the approval of multiple ethics committees, each with its own requirements and working with different timings;
3. Still for multicentre trials, the for the authorization from multiple committees and people, as for example clinical councils, surgery coordinators and local research committees;
4. Absence of the specific legal statute for being PhD Student and Senior Doctor (as it exists for trainees);
5. The fact of PhD being very expensive;
6. The lack of acknowledgment for research skills as something that should be done by doctors in the Portuguese NHS;
7. The overwhelming clinical workload given to doctors, namely the younger ones.

Frederico Rosário, in turn, highlighted three measures he believes could help changing the clinical research panorama in Portugal:

1. Acknowledgment of the importance of research, namely by providing doctors with time for it and giving support to get education for research;
2. Faster timings for the approval of trials (by Ethics Committees and CNPD);

3. Availability of staff dedicated just to give support to statistics work as well as helping out on the design and analysis of the trials.

Tiago Sousa Veloso also pointed out three possible solutions:

1. Faster timings for the approval of studies;
2. Full implementation of the rules for the legal statute of the registrar-PhD student, not forgetting mechanisms for support of research,
3. Discourage research just for curriculum purposes and instead promote quality research.

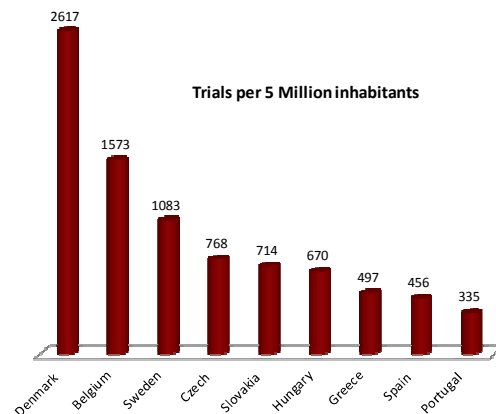


Figure 2– Clinical Trials in Europe - Portugal at the European Bottom (Source: ClinicalTrials.gov consulted Jan. 2012 for Year 2011)

Impeding the conduction of clinical trials, the obstacles are enormous and seem almost insurmountable at times:

- Absence of a structured strategy for clinical research;
- Weak education in the research field;
- Absence of structured teams;
- The pressure to see the maximum number of patients;
- The excessive time spent in bureaucratic activities;
- The lack of support personnel;
- The lack of infrastructures;
- The lack of financial incentives;
- No clear rules for compensation of the time invested in research;
- The bureaucracy dealing with Infarmed, CEIC or CNPD (Comissão Nacional de Protecção de Dados - Data Protection National Commission) - too overwhelming for the time available to doctors, especially for those outside Lisbon who cannot deal

directly with the regulatory managers at Infarmed, CEIC or CNPD. The process is slow and with too many obstacles.

Doctors willing to do investigator-initiated (academic) clinical trials are mostly on their own. There are:

- No clinical research unit, infrastructures, or meaningful support at most health units;
- No statisticians on staff to help;
- No IDS pharmacists;
- No research nurses;
- No database managers;
- No regulatory affairs managers;
- No pharmacovigilance managers;
- No marketing recruiters;
- No monitors;
- No administrative assistants;
- No funds to hire CRO to compensate for lack of all the above;
- No funds for regulatory approval fees;
- No insurance funds;
- Etc.

Strategies for promoting primary care research in less economically developed countries like Portugal, should take into account the fact that clinicians are often overwhelmed by clinical demands in truly chaotic systems. (W. Beasley, Starfield, van Weel, W. Rosser, & L. Haq, 2007) The political agenda is to pressure ARS and ACES executive directors to increase the number of visits and number of listed patients per doctor.

Another important issue to deal with is the suspicion by some good doctors that all industry clinical trials are biased and automatically “not relevant”. The truth is that, with regulation, pharmaceutical industry has a word to say and contributes to very meaningful research.

In Portugal, only with great perseverance can a family doctor go forward with a clinical trial. Leaderships usually see clinical research as a secondary aspect. Even medical education is many times seen as useless for the quality of the service they rule. The big focus for management is almost inevitably on the clinical activities. Patients must be seen and that’s basically almost everything. Going against this ingrained way of thinking is “very tiring”.

The isolation of primary care from the academic health centre, the usual site for clinical research, appears to further aggravate the delay between the discovery of new research findings and the adoption of those findings into practice. (Peterson, 2006)

Armando Brito de Sá, from Faculdade de Medicina da Universidade de Lisboa states that one of the current problems with Portuguese family medicine research lies in the fact that an academic career is not as attractive as it should be, mainly for financial reasons. For him, fields of public recognized importance must be identified. The identified themes would be the guidelines for future clinical research in family medicine, so that governments feel it is important to finance it. Research lines are urgent to be established and followed. If the

promoter is academic or industry related is not important for him. Interaction is even possible as far as it is transparent, with well defined goals and deadlines.

4.1.5 Opportunities

Portugal also has positive points that can foster clinical research. One of it is the fact of Family Medicine trainees usually being encouraged to do more than medical consultations. Unfortunately, once a doctor becomes a specialist in Family Medicine, he no longer has the same flexibility to manage his non-clinical work. We can make research education more solid and give trainees a more supportive context to grow after the vocational training.

Also positive the fact that In Portugal there are many patients from ethnic minorities in certain health centres. They are attractive for the pharmaceutical companies which desire to test drugs in representative samples of the general population.

It is important to underline other relevant opportunities like the ones promoted by ECRIN (European Clinical Research Infrastructures Network), PtCRIN (offspring of ECRIN) or PNEC (INFARMED drug agency's clinical trials platform).

It is also not negligible recent funding and training programs for clinical research.

Besides, the lack of support to health units and investigators wishing to conduct clinical trials can be addressed by creating a network of academic CROs. Academic CRO's like Nova Medical School CRU - Clinical Research Unit can support academic clinical trials of doctor investigators from Nova's affiliated teaching health units and PtCRIN.

4.1.6 Three Cases of Clinical Trials in the Portuguese Family Medicine

By 2006, one of the first clinical trials in a primary care setting was done in Portugal. It was at Centro de Saúde da Lapa, in Lisbon. The pharmaceutical industry was the sponsor. GlaxoSmithKline (GSK) was the one, doing it in an international clinical trial for its vaccine for the human papiloma virus (HPV). According to Alexandra Bordalo (from GSK), during a conference in 2006, one of the most complex and time expending issues was the financial contract. Those issues were responsible for a significant delay in the beginning of the subjects' recruitment in the Portuguese sites due to heavy bureaucracy.

In 2012, there was a Phase III clinical trial with empagliflozin promoted by Boehringer-Ingelheim. This molecule was being tested for Diabetes Mellitus and one of the research sites was USF Santo André de Canidelo (ACES do Grande Porto VIII – Gaia). By the time the Unit was approached for this thesis, Fernando Ferreira was the coordinator of that primary care unit in the Portuguese National Health Service. According to him, one of the main difficulties emerged from the generalized doubt about their capacity to participate in this clinical trial. Also, bureaucracies with the local ACES, ARS, CEIC and Infarmed were a problem.

Once more the time for obtaining answers from those institutions was too lengthy and when that happens, opportunities are simply lost.

According to Fernando Ferreira, the clinical research education is not accessible to everyone. He says not all the health units have infrastructures or material and not all the work teams feel motivated to work in clinical research doing phase II or III clinical trials.

Also, the absence of financial protocols that provide justice and equity in the distribution of economic benefits for all the institutions and researchers involved is a serious unresolved problem.

Fernando Ferreira stated that bureaucracy must be dramatically reduced. All the documentation and authorization process must be accelerated and a group of Units with researchers must be developed. Education in clinical research must be enhanced and justice and equity for getting financial benefits must be guaranteed.

In 2013, USF Santo André do Canidelo was expecting to begin a new clinical trial. Then, this unit was to be accompanied by three other sites in the Portuguese Primary Care context. It would be for a double-blinded clinical trial with two active drugs and a placebo. It would also be for Diabetes Mellitus.

For Family Doctors who had already any previous experience with clinical trials it was created a second questionnaire that would be answered only by José Augusto Simões. This family doctor works at USF Marquês de Marialva, in Cantanhede (central region of Portugal).

The sponsor for this clinical trial experience was Boehringer Ingelheim and it was asked for three major obstacles and three strategies to overcome the obstacles.

About the three major obstacles, José Augusto Simões would say:

- ARS authorizations;
- Need for the implementation of an ethics committee at ARS;
- Effort of the remaining professionals of the unit.

About three strategies to overcome the obstacles, José Augusto Simões stated:

- Phone calls clarifying doubts and pressuring the authorizations;
- Elaboration of a concrete proposal for the constitution of an ethics committee;
- Reunions for clarifying and provide training in good clinical practice.

4.2 Current European Strategies to Increase Clinical Trials

Researchers and practitioners stand to gain considerably from an integrated approach. (Thomas, Graffy, Wallace, & Kirby, 2006) Shared projects help participants to develop trusted relationships.

Networks may reduce the work involved in developing partnerships because they reach into many organizations and institutions. (Thomas, Graffy, Wallace, & Kirby, 2006) This will not only benefit the academic research, the one promoted by the investigator, moved only

by the scientific spirit, but also the pharmaceutical industry promoted research. It will be much easier to establish protocols for multicentre studies.

Primary care (and so family medicine), by its comprehensive nature, relates to other disciplines both inside and outside of medicine (e.g. sociology, anthropology, health economics, and industrial engineering); primary care researchers benefit through collaborations with each of these different fields of knowledge. (W. Beasley, Starfield, van Weel, W. Rosser, & L. Haq, 2007).

That's why EU organisms have a role to play. Below are mentioned some of them:

- European Centre for Disease Prevention and Control (ECDC);
- European Food Safety Authority (EFSA);
- European Institute of Innovation and Technology (EIT);
- European Medicines Agency (EMA);
- European Monitoring Centre for Drugs and Drug Addiction (EMCDDA);
- European Research Council (ERC);
- Executive Agency for Health and Consumers (EAHC);
- Research Executive Agency (REA).

As referred by Van der Zee, Kroneman and Bolibar in 2003, in order to obtain better results in clinical research it must be assured the existence of:

- Scientific associations;
- Peer-reviewed journal(s);
- Defined population(s) resulting in population denominator(s) for practices;
- A system for linking primary care to other health care services;
- Departments and chairs of general practice at universities;
- Integration of educational and research centres;
- Clinicians working in group practices or health centres;
- A certain degree of independence from the government;
- Financial support for practicing clinicians to conduct research.

In order to have high quality applied clinical research in primary care, Kekki in 2005 summarizes it with the next three items:

- Supportive climate;
- Motivated researchers;
- Adequate funding.

A supportive climate is acquired with protected time for research functions, infrastructures and support staff availability.

With supportive climate, it will be easy to find motivated researchers in a highly qualified and scientifically prepared generation of doctors who are embracing family medicine as their professional project of life.

About adequate funding, in the current political and financial context Europe lives, from the public budget this will probably be hard to get. Instead, it can be found in the pharmaceutical industry or foundations.

4.2.1 European Networks

Portuguese family medicine is connected with the European General Practice Research Network (EGPRN), an organization of General Practitioners / Family Doctors and other health professionals involved in research in primary care and family medicine. This network is part of the WONCA Europe structure and helps the collaboration and changing of ideas between researchers all over Europe.

In fact, EGPRN already developed a Research Agenda for General Practice / Family Medicine and Primary Health Care in Europe which was written upon request of WONCA Europe.

The Research Agenda focus in the main competencies and characteristics of Family Medicine, stating research needs and main action points.

Below are the seven main topics worked out in this agenda:

- To further develop and evaluate generic (person-centred, bio psychosocial, comprehensive or community-based) models or strategies;
- To encourage comparative research in populations with different cultural, social, or geographic contexts and healthcare systems;
- To promote and support longitudinal cohort studies to evaluate the prognosis and determinants of health and disease;
- To promote and support intervention studies and randomized controlled trials which take into account broad issues such as patient preferences, multimorbidity, quality of life and social and environmental circumstances;
- To encourage research focusing on diagnostic strategies and reasoning;
- To promote studies assessing effectiveness and efficiency in everyday care;
- To develop and validate functional and generic instruments and outcome measures for use in GP/FM research and care.

While this research agenda does not put clinical trials as a priority, it still has to be a reference to take into account whenever we think about research.

Finally, the European Clinical Research Infrastructures Network (ECRIN) is an infrastructure supporting multinational clinical research projects all over Europe. This, not being specifically for family medicine context, can also be useful since it is an infrastructure that can help when trying to do multinational clinical research. ECRIN provides help to investigators and sponsors in preparing and conducting multinational clinical studies. That can be of great help because there are problems that are common to all the European countries.

4.2.2 The United Kingdom Case

United Kingdom seems to be some steps ahead when we talk about clinical research in family medicine. With a National Health Service similar to the one Portugal has, it would always be important to look at. UK Primary Care clinical trials are developed in research networks. They have developed primary care research infrastructures that have been enabling and influential internationally. (Sullivan, Butler, Cupples, & Kinmonth, 2007) That's how multiple relatively small health units interact to bring up good science. Research networks offer a managed approach to hosting high quality research in the health service assuring recruitment and retention of study participants. (Sullivan, Butler, Cupples, & Kinmonth, 2007) This approach is apparently giving good results. Making part of a wider initiative, it was established one primary care research network for the whole country, which includes six topic specific networks and a comprehensive clinical research infrastructure through which service support, research governance, and academic staff is funded. (Sullivan, Butler, Cupples, & Kinmonth, 2007)

The England wide primary care research network comprises central coordination for eight distinct local networks, like it could be done in Portugal. These networks link interested practice teams and local academic units of general practice to participate in a wide range of national projects led from the service, universities, and industry. (Sullivan, Butler, Cupples, & Kinmonth, 2007)

Additionally, a National School for Primary Care Research was established in 2006. (Sullivan, Butler, Cupples, & Kinmonth, 2007) This was for sure a good step to stimulate research in this context and carries, of course, an important intrinsic signal – primary care research is crucial and there's the intention to support it. From prevention to the management of long-term conditions, all the phases of health intervention are worked in England. Recruitment and retention strategies are also studied.

Different ways of organising the networks will always be associated with different outcome profiles. A top-down, hierarchical approach based on institutional alliances and academic expertise attracts more funding and appears to be stable. The bottom-up, individualistic network with research practices is good at reflecting on practical primary care concerns. (Thomas, Graffy, Wallace, & Kirby, 2006) Both are defensible and have their own advantages.

From June 2013 to May 2014, I worked in Northern Ireland which as part of the UK was an opportunity to better understand the UK reality. Although I worked in the secondary care, I couldn't avoid noting the fact that it was very easy to get additional training in Good Clinical Practice. I was involved in a Clinical Trial in the field of Rheumatology and just before starting I easily had access to an Online Course with good quality training support. The Online option was a fine solution which turned out to be beneficial for the flexible schedule offered. I didn't have to go anywhere and my learning rhythm was respected.

4.3 Questionnaires on Family Medicine Clinical Research

4.3.1 “Portuguese GPs and the Clinical Trials Questionnaire – 2012”

In order to understand and confirm whether identified problems and opportunities are indeed relevant to Clinical Research in the Portuguese family medicine context, a questionnaire entitled “Portuguese GPs and the Clinical Trials” (see attachment at the end of the thesis) was submitted in 2012 to family medicine specialists and trainees through e-mail based Portuguese family medicine forums (MGF XXI; MGFamiliar; EURACT-PT) These had the clear goal to characterize how Portuguese family doctors feel about Clinical Trials.

Below, its results are described and analyzed from a total of 21 answered questionnaires. Two of the answered questionnaires were only partially completed, even in the “yes/no” questions, probably by distraction of those specific doctors. Two other doctors didn’t answered for one or another specific “yes/no” question, probably also by distraction. Most of the doctors didn’t answer to the open ended questions.

Table 1 – Sample Characterization

| | Male | Female |
|---------------------|--------------------|-------------------|
| Gender | 9 (43%) | 12 (57%) |
| | Trainee | Specialist |
| Career Stage | 9 (43%) | 12 (57%) |
| | Until 45 Years Old | Over 45 Years Old |
| Age | 15 (71%) | 6 (29%) |

As it is clear by table 1, answers were obtained from a balanced gender and career stage sample. Most of the responders were below 45 years old.

In the questionnaire there were twelve simple “yes/no” questions. Below, they are organized as they were stated in the questionnaire.

1. Did you ever have an interest in conducting clinical trials?
2. Are you aware of the regulatory requirements to conduct a clinical trial?
3. Do you know how to deal with the experimental drug during a trial?
4. Do you know what documents to submit to seek clinical trial approval?
5. Do you know what good clinical (for research) practices are?
6. Do you know the main rules and regulation to abide by during a clinical trial?

7. Do you know what requirements you must fulfil to close a clinical trial?
8. Do you know where to go to educate yourself about such requirements?
9. Does your health centre have infrastructures for conducting clinical trials?
10. Would an academic career in clinical trials fulfil your role as a GP?
11. Do you think that the country can benefit from clinical trials?
12. Do you think the health system can benefit from clinical trials?

As it is possible to confirm by the data presented, there is interest in conducting clinical trials.

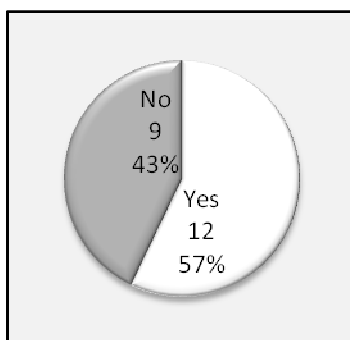


Figure 3– Did you ever had an interest in conducting clinical trials?

Even less than 50% referring to be aware of the regulatory requirements to conduct a clinical trial, 43% is not that bad.

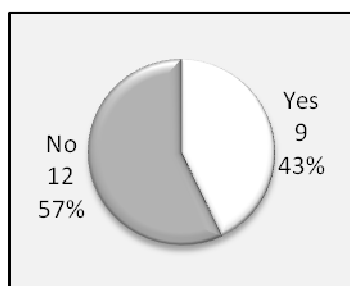


Figure 4 - Are you aware of the regulatory requirements to conduct a clinical trial?

Much more problematic is the fact that only 19% assume being certain that they know how to deal with regulations during a trial. Fortunately this for sure is an issue that can be resolved.

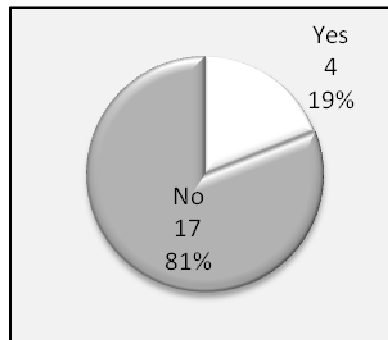


Figure 5 - Do you know how to deal with the experimental drug during a trial?

From this questionnaire, it seems that most family medicine specialist/trainees also don't know what documents to submit in order to approve a clinical trial (76%).

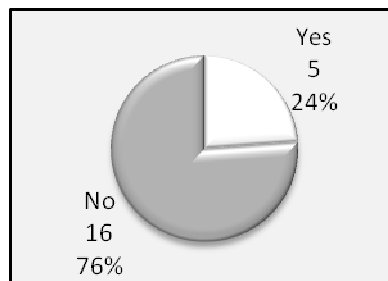


Figure 6 - Do you know what documents to submit to seek clinical trial approval?

Figure 7 presents interesting data.

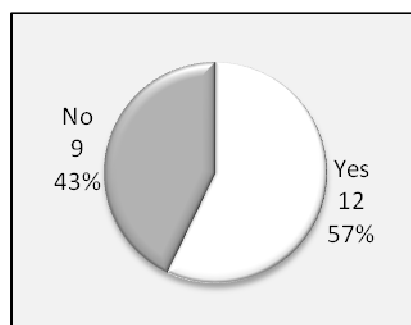


Figure 7 - Do you know what good clinical (for research) practices are?

Truth or not, a considerable number of family medicine specialists/trainees refer that they are aware of the Good Clinical Practices for research. There is the possibility of confounding Good Clinical Practices for research with others much more disseminated through family medicine doctors and related with the clinical work.

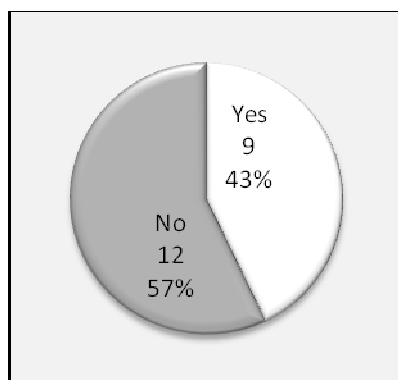


Figure 8 – Do you know the main rules and regulation to abide by during a clinical trial?

The actual education and training given about research is still not enough. Clearly there is a lack of theoretical knowledge about the requirements to fulfil in order to close a Clinical Trial. From the ones who affirm to know, how much can really put in practice this knowledge, since their experience in clinical trials is scarce or simply none?

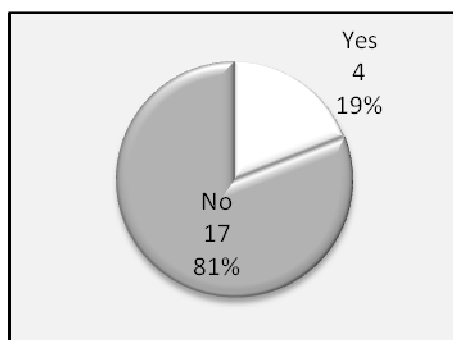


Figure 9 - Do you know what requirements you must fulfil to close a clinical trial?

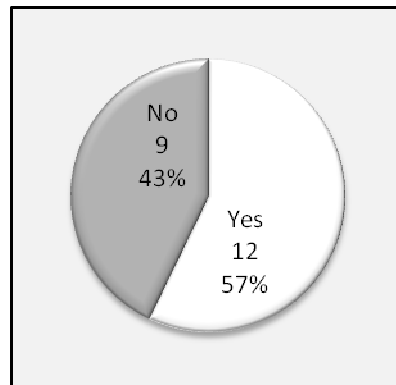


Figure 10 - Do you know where to go to educate yourself about such requirements?

A considerable number (57%) state knowing where to get training, but probably are not motivated for education since in the next immediate question, 81% assume they don't have any infrastructures in their workplace to help them develop research.

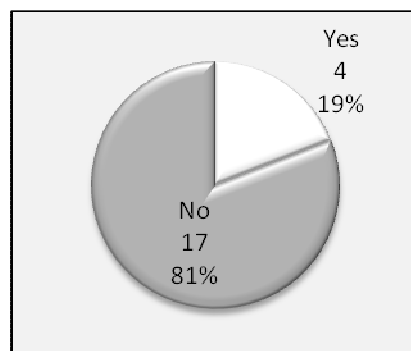


Figure 11 - Does your health centre have infrastructures for conducting clinical trials?

On a positive note, not having infrastructures to conduct clinical trials does not precludes doctors from totally excluding clinical research, since 43% believe an academic career in clinical trials could be interesting.

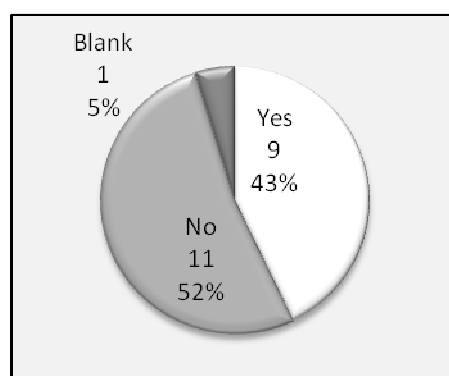


Figure 12– Would an academic career in clinical trials fulfil your role as a GP?

There was not a single negative answer to the eventual benefit of clinical trials to the country, which means that it is accepted that by improving clinical trials, Portugal itself evolves.

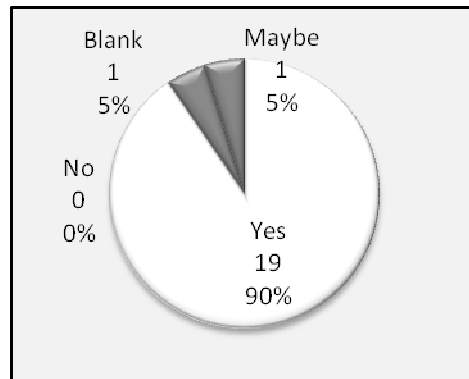


Figure 13 - Do you think that the country can benefit from clinical trials?

What about the health system? Equal to the above question.

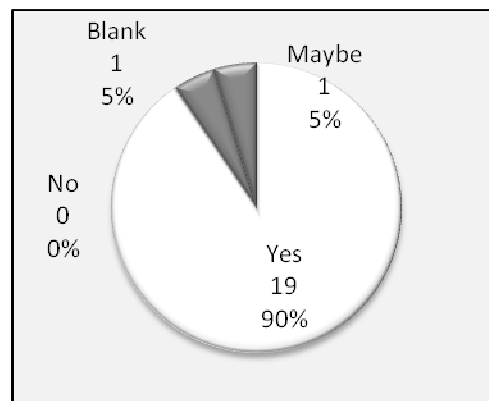


Figure 14 - Do you think the health system can benefit from clinical trials?

After the first twelve questions, I asked about agreement or not about some possible obstacles for doing clinical research. Once more, a “yes/no” answer was asked for. Below, I enumerate the possible obstacles to clinical research:

- Pressure to see the maximum number of patients;
- Lack of support personnel;
- Lack of financial initiatives;
- No clear rules for compensation of the time invested in research;
- The bureaucracy dealing with INFARMED, CEIC or CNPD - too overwhelming for the time available to doctors, especially for those outside Lisbon who cannot deal directly with the regulatory managers at INFARMED, CEIC or CNPD;

- Once a doctor becomes a specialist in family medicine, he no longer has flexibility to manage his non-clinical work.

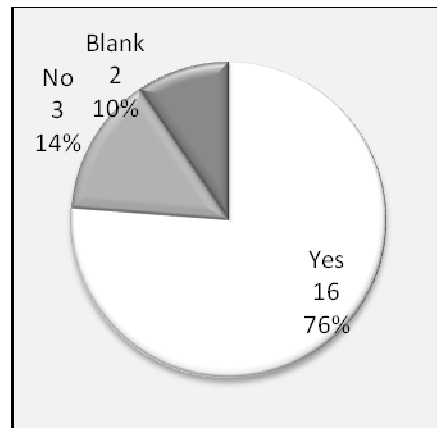


Figure 15 - Pressure to see the maximum number of patients

Most family doctors agree with the identified obstacles for clinical research.

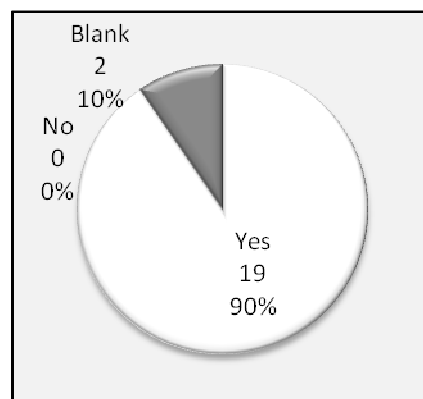


Figure 16– Lack of support personnel

As can be seen above, all the answering doctors agreed with the lack of support personnel obstacle.

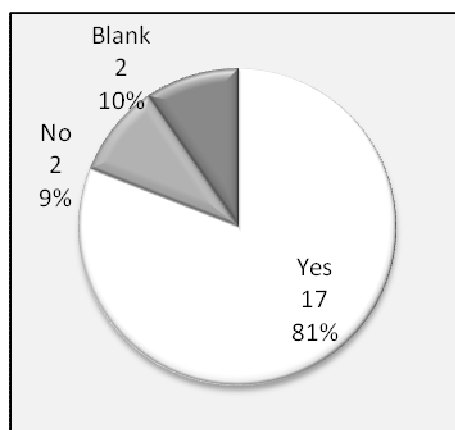


Figure 17– Lack of financial initiatives

The same happened when asked about the obstacle related with not existing rules for compensation for the work invested in research.

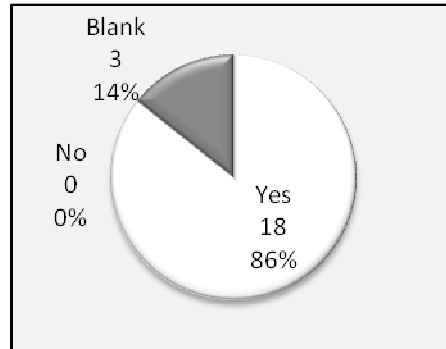


Figure 18 - No clear rules for compensation of the time invested in research

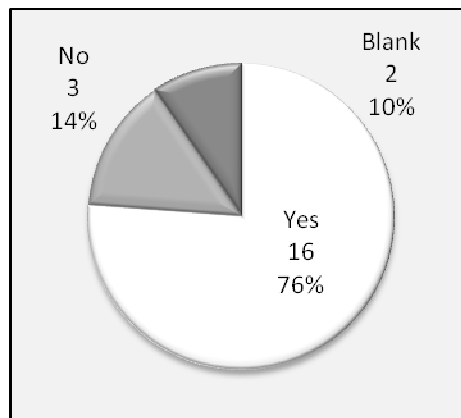


Figure 19– The bureaucracy dealing with INFARMED, CEIC or CNPD - too overwhelming for the time available to physicians, especially for those outside Lisbon who cannot deal directly with the regulatory managers (...)

The bureaucracy is clearly seen as an obstacle. Curiously, the answers about the non-flexibility to manage non-clinical work after internship were very balanced.

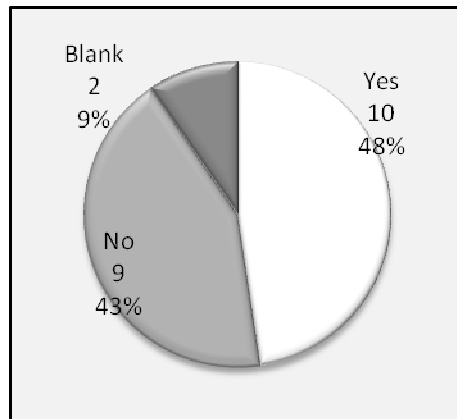


Figure 20 - Once a doctor becomes a specialist in family medicine, he no longer has flexibility to manage his non-clinical work

After this sequence, it was asked for any other obstacle that possibly could be important to that specific family medicine specialist/trainee.

In this respect, it was obtained six answers as additional obstacles:

- Even prior to becoming a specialist, as a trainee, it is hard to reconcile schedules of “clinical work”, “academic work” and family life”;
- Patients’ compliance and no support from other doctors (colleagues) – colleagues say that they would never support another colleague that would like to do research if that were to interfere on “pay-for-performance style of a USF Model B”;
- Her own preference in doing clinical work;
- The division of time between university work and clinical work and the salary gap between the two careers, making research unattractive;
- Lack of knowledge about this subject;
- Whole team mindsets regarding feasibility of clinical trials in primary healthcare.

In the “Portuguese GPs and Clinical Trials Questionnaire” which was done for this Master of Science Thesis in the beginning of November 2012, there were also questions about possible solutions or recommendations to improve clinical research in Portugal, as it is stated below:

- To put Clinical Research and particularly Clinical Trials in the political agenda;
- To establish a system of effective communication between clinical units and GP academic departments;
- To delegate some routine family physician functions to other health professionals in order to gain physician’s space and time for research and therefore not compromising the number of patient visits;
- To contracting support staff (statisticians, nurses, administrative, etc.) specifically for research;

- To improve cooperation between clinical units and family medicine university departments;
- To involve health care units in education and research networks;
- To give economical independence to health centres;
- To finance the practicing clinicians in order to conduct research; having protected time and being paid to work on studies;
- To obtain industry funds in a non-binding way to increase funds and support rooms, better equipment, even newer equipment, furniture, refurnishing walls, computers, without sacrificing the available budget.

Again, the asked answers were “yes/no” ones. The results are below:

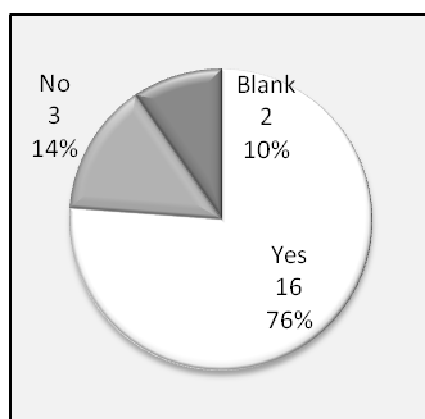


Figure 21 - To put Clinical Research and particularly Clinical Trials in the political agenda

The majority agrees with the importance of bringing clinical research and particularly clinical trials to the political agenda.

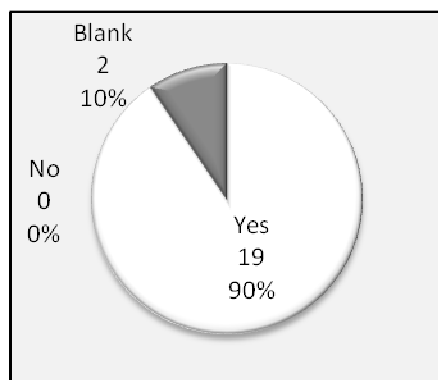


Figure 22 - To establish a system of effective communication between clinical units and GP academic departments

All the obtained answers were favourable to establishing a system of effective communication between clinical units and GP academic departments.

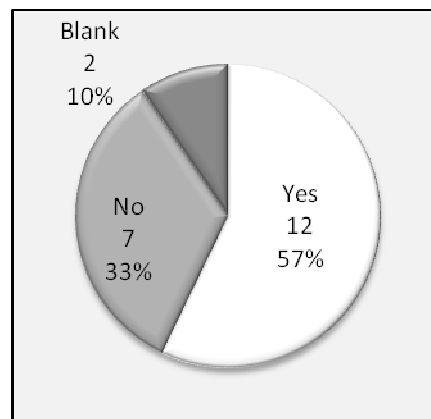


Figure 23 - To delegate some routine family physician functions to other health professionals in order to gain physician's space and time for research and therefore not compromising the number of patient visits

A less expressive support was obtained to the possibility of delegating some routine family doctor functions to other health professionals. This probably reflects some apprehension due to recurrent and inconsequent attempts from nurses to get functions clearly not being qualified for that.

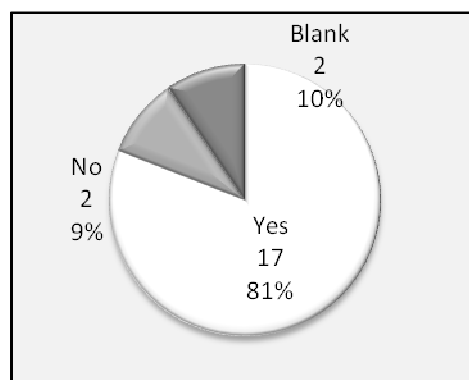


Figure 24 - To contracting support staff (statisticians, nurses, administrative, etc.) specifically for research

As it can be seen above, contracting support staff is positive for most of the responders.

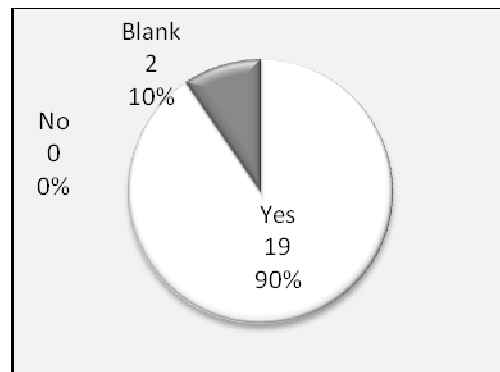


Figure 25 - To improve cooperation between clinical units and family medicine university departments

It was unanimous the support for improvements in the cooperation between clinical units and family medicine university departments. The same happened for the involvement of healthcare units in education and research networks.

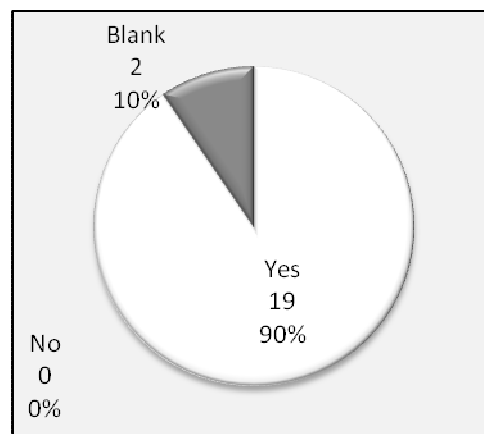


Figure 26 - To involve healthcare units in education and research networks

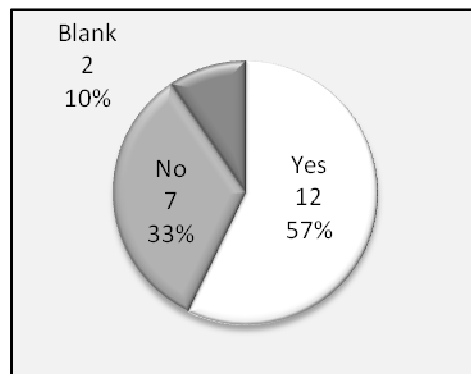


Figure 27 - To give economical independence to health centres

Curiously, receiving economical independence for the health centres wasn't seen in such a unanimous way as it could be expected. 33% of the responders answered "No".

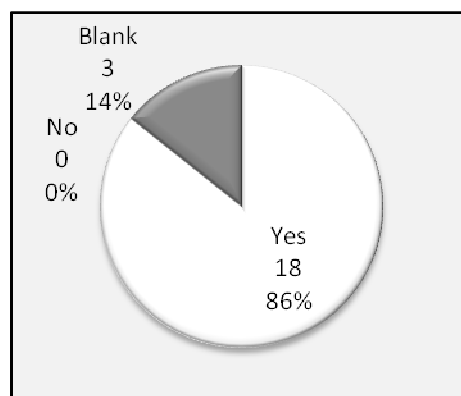


Figure 28 - To finance the practicing clinicians in order to conduct research; having protected time and being paid to work on studies

Unanimous was the answer to the possibility of receiving financial support specifically for conducting research and having protected time to work in studies.

Obtaining industry funds was an option against which 52% answered, probably reflecting the scepticism, distrust and even demonization of the pharmaceutical industry between the Portuguese family doctors.

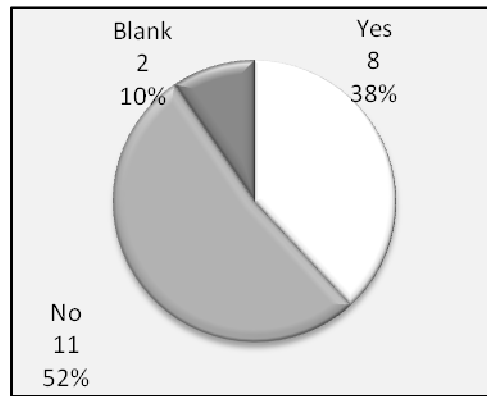


Figure 29 - To obtain industry funds in a non-binding way to increase funds and support rooms, better equipment, even newer equipment, furniture, refurbishing walls, computers, without sacrificing the available budget

After this, it was asked for any other suggestions to improve clinical trials in a primary care setting. And for this question I would find only one answer:

- Strong GP university departments, fully staffed, adequately paid, linked to collaborating health centres, both for teaching and research.

Asked about the possibility of once more getting involved in a Clinical Trial, the answer was “yes”.

4.3.2 “Portuguese GPs and Clinical Trials Questionnaire – 2014”

In June 2014 another questionnaire was applied to family doctors and family medicine trainees from Portugal. This time, it was chosen to make a much simpler questionnaire in order to maximize the number of answers.

It used online forums (MGFamiliar, MGF_XXI, MGFClinica, EURACT-PT), emails and the social network Facebook.

There was no formal document and the questions were directly typed in the emails and on Facebook.

Five questions were asked and 84 family doctors / family medicine trainees replied.

It must be underlined that the answers were restricted to values between 0 and 20.

The first question was the following:

1. In a weekly work schedule of 40 hours, how many would you like to have just to work on Clinical Trials?

Table 2 – Statistical Analysis for the answers to Question 1

| | |
|--------------------|-------|
| Number of Answers | 84 |
| Maximum | 20 |
| Minimum | 0 |
| Mean | 4.411 |
| Mode | 5 |
| Median | 4 |
| Standard Deviation | 3.675 |

As you may well see on the table above, with a standard deviation of 3.675, the mean was 4.411. Mode was 5 with the answers ranging from 0 to 20. Generally, it seems that once a week doctors would like to have a period of 4 to 5 hours to dedicate only to clinical trials.

The next question was:

2. Classify the importance that Clinical Trials should have in the daily work of a Family Doctor.

Table 3 - Statistical Analysis for the answers to Question 2

| | |
|--------------------|--------|
| Number of Answers | 84 |
| Maximum | 20 |
| Minimum | 1 |
| Mean | 11,387 |
| Mode | 15 |
| Median | 11 |
| Standard Deviation | 5,018 |

On the above table is quite clear that with a standard deviation of 5.018, the importance of Clinical Trials for Portuguese Family Doctors is something that tends to be variable. The mode was 15, which is quite high, but the mean was 11.387.

Below is the third question:

3. Classify how much do you agree with the use of scientific paper publication as criteria in the assessment of the Family Doctors

Table 4 - Statistical Analysis for the answers to Question 3

| | |
|--------------------|--------|
| Number of Answers | 84 |
| Maximum | 20 |
| Minimum | 0 |
| Mean | 11,488 |
| Mode | 10 |
| Median | 10 |
| Standard Deviation | 5,128 |

The pattern of the answers is similar to the one observed for question 2 with one major difference. The mode here was 10. An hypothesis for this decrease, is the possible notion that in the current context, with the current conditions, scientific paper publication is very hard for a Family Doctor. Caring of the patients is their main role and the leaderships don't really support doctors to routinely publish papers.

Below is the fourth question:

4. For the assessment of the Health Centre where you work, how much would you agree to have Clinical Trials development as criteria?

Table 5 - Statistical Analysis for the answers to Question 4

| | |
|--------------------|--------|
| Number of Answers | 84 |
| Maximum | 20 |
| Minimum | 0 |
| Mean | 10,756 |
| Mode | 15 |
| Median | 10 |
| Standard Deviation | 5,497 |

In the above question, the observed pattern presents with an even higher standard deviation. Mode is once again 15, but the mean has a mild decrease.

The last question is below;

5. If you had the support from the leaders of the Portuguese National Health Service and also a suitable structure, with how much motivation would you work on Clinical Trials?

This is the question that would finally say what could happen in ideal conditions. The question intended to underline what would be the receptivity of Family Doctors to a change in the conditions for the work on Clinical Trials given by the Government of Portugal.

Table 6 - Statistical Analysis for the answers to Question 5

| | |
|--------------------|--------|
| Number of Answers | 84 |
| Maximum | 20 |
| Minimum | 4 |
| Mean | 15,762 |
| Mode | 20 |
| Median | 17 |
| Standard Deviation | 4,428 |

Mode was an impressive 20 for a mean of 15.762. The Government of Portugal may well count on Family Doctors to collaborate if they choose to invest on the creation of suitable conditions for an improvement of the Clinical Trials panorama in Portuguese Family Medicine.

4.3.3 “Improving Clinical Trials in Portuguese Family Medicine” – The Vision of 15 Key Opinion Leaders

Some Key Opinion Leaders were approached with the following question:

List 3 ideas that should be implemented in order to improve the development of Clinical Trials in the Portuguese Family Medicine.

Below it's presented a table with the answers of the fifteen who accepted to collaborate and replied.

Table 7 – The answers of the 15 Key Opinion Leaders Approached

| Key Opinion Leaders | Three ideas to improve the development of Clinical Trials in the Portuguese Family Medicine. |
|--|--|
| Dr Fernando Ferreira (Coordinator of USF Santo André do Canidelo) | Good Clinical Practice Training |
| | Developing Research Networks |
| | Paying for the research work |
| | Speeding up the bureaucracy |
| Dr Denise Alexandra (Current Portuguese EURACT Council Member) | Logistical support from the Ministry of Health, e.g. Protected time for Clinical Trials |
| | Financial support from the Ministry of Health, eventually with honest and transparent partnerships with the Pharmaceutical Industry |
| | Training for the professionals who want to do research |
| Dr Luís Filipe Gomes (Former Portuguese EURACT Council Member) | Learning of research during vocational/specialty training |
| | Relevance of research in CME/CPD schemes |
| | Time and money allocated for researchers |
| | Change of publishing politics |
| Dr Vítor Ramos (Invited Assistant Professor at ENSP) | There must be a clear National framework and guidelines |
| | There must be a National regulatory entity or regulatory body |
| | There must be enough independency in relationship to industry, mediated technically and in financial aspects by the National regulatory body |
| Professor Luíz Miguel Santiago (Invited Associate Professor at UBI) | Strategic and population aim of scientific knowledge |
| | Infra-structural improvement of the Primary Care Units |
| | Through fees improve the quality and the number of devoted scientists in the Primary Care setting |
| Professor António Vaz Carneiro (Professor at FMUL / Director of CEMBE) | Protected time for research for Family Doctors |
| | Direct financing for research in primary care |
| | Creation of CROs in Primary Care |
| Dr José Silva Henriques | To sensitize the Ministry of Health for the importance of Clinical Research in Family Medicine Units, as it is essential for the quality of practice |

| | |
|--|---|
| (President of the College of Family Medicine at Ordem dos Médicos) | To Promote next to Family Doctors, the importance of Clinical Research for quality, continuous improvement and advance of clinical practice |
| | To give time for Research, namely by inserting it in the Family Doctor work schedule, for those who take on the role of researchers in their Health Units |
| Dr Raquel Braga (Former Editor at RPMGF) | Ethic discussion about clinical trials in Primary Care |
| | Time and resources for the subject (financial and other) |
| | Training only for those who are interested |
| Professor José Manuel Silva (President of Ordem dos Médicos) | Greater importance of Clinical Research in Family Doctors' CV |
| | Allocation of time for research |
| | Elimination of excessive bureaucracies and speeding up response times by the involved entities |
| | Financial retribution |
| Dr Luís Pisco (Vice-President of ARS de Lisboa e Vale do Tejo) | To promote training in clinical trials management, namely about defining timings, mechanisms and defining the structure and the logistics needed for the development of Clinical Trials in Primary Care at each Health Unit, trying to adapt the resource for clinical trials in this setting; |
| | To promote pragmatic clinical trials adequate to the reality of Primary Care and to the needs in Health, in particular effectiveness of the interventions in Health; |
| | To promote clinical research oriented for the interests of the National Health Service and of the Health professionals namely through the creation and financing of support offices to Clinical Research in the ACES, through the harmonization of the care and research needs, the empowerment of the human and material resources for the development of that activity; |
| | Integration of the Primary Care Health Functional Units in national and international research networks in Primary Care, divided by thematic classes like respiratory diseases, arterial hypertension, depression, diabetes and musculoskeletal diseases; |
| | To establish objective conditions to receive clinical trials promoted by the Pharmaceutical Industry, through the creation of cooperation and partnership protocols between the Regional Health Administrations, Pharmaceutical Companies and CROs encouraging activities which give gains in training and clinical excellence for the professionals (at ARSLVT). |
| Professor Jaime Correia de Sousa (Professor at Escola de Ciências da Saúde da Universidade do Minho) | Family Health Units should be able to contract protected time for research, including CT with the Health Services Management. |
| | One or more members of the practice team should be in charge of promoting and managing research that should involve the whole team. |

| | |
|---|---|
| | A National (or Regional) Institute of Primary Health care should be created aiming at Specific Training of Primary Health Care professionals, CME / CPD and Research. It should be closely associated with Academic Departments of Family or Community Health in Medical and Nursing Schools. |
| Dr José Miguel Guimarães (President of the North Regional Section of Ordem dos Médicos) | To speed up the approval of Clinical Trials in Portugal, namely by professionalizing a National Ethics Committee that analysis and replies within suitable timings and deadlines. |
| | To establish Clinical Research time in the doctor's schedule, e.g. 5 hours weekly, just for Clinical Research, namely Clinical Trials. |
| | To value adequately Clinical Research (including Clinical Trials) within the doctors' Curriculum Vitae (namely while recruiting) and within a Health Unit. |
| Professor José Augusto Simões (President of ADSO) | Good Clinical Practice Courses, for Clinical Trials, open to Family Medicine Trainees and Family Doctors. |
| | Creation of one Clinical Trials' Unit at each ACES |
| | Development of a structure at each ARS to deal with Promoters about everything related with Clinical Trials. |
| Dr Carlos Martins (Founder of the Website MGFamiliar.net) | Training in pragmatic research design and methodology |
| | Training in medical statistics |
| | Offering support of statisticians to primary healthcare researchers |
| Professor Armando Brito de Sá (Professor of Family Medicine at FMUL) | A real payment, not included in the salary, just for family doctors who work on Clinical Trials, not dependent on absurd overheads established by the Ministry of Health. |
| | Allocation of legal protected time for research in the profile of a Family Doctor (4-6 hours weekly). |
| | Acknowledgment, for a small number of Family Doctors, from the academic career of Family Medicine, permitting investment of time in the academic area without losing money (e.g., 7-8/10 of the week schedule dedicated to the academic area and 2-3/10 of the week schedule dedicated to clinical work). |

5. Discussion

Clinical Trials are very scarce in Portuguese Family Medicine but in the twenty first century you cannot isolate the Portuguese case from the rest of the European context.

In literature review it was detected a networks model used in the United Kingdom and in the rest of Europe. Networks can help integrate academic research and service development initiatives by facilitating inter-organisational interactions.

With research networks in Portugal linked between each other, included in a nationwide network and also interacting with equivalent ones from everywhere in the world we will be taking a step forward in order to increase the quantity and quality of Portuguese clinical research, particularly in the Family Medicine field. Clinical trials will be no exception.

The mentioned European networks are essential for the success of Portuguese Family Medicine research. That's also why we must send Portuguese representatives to the European existent structures. Our representatives can go and bring more knowledge and skills. Interacting with more experienced colleagues can also be a way of surpassing years of delay.

Analyzing the questionnaires previously described, it is clear that while Family Doctors fear delegating some functions that are exclusively done by them, it is also true that they are very keen about the possibility of being more involved in research activities as Clinical Trials. It seems that while on the current context they effectively don't do much research work, if the suitable conditions were provided and problems were corrected, they would in fact be happy to have hours on their own weekly schedule just for research.

From the answers provided by the Key Opinion Leaders approached, it is easily understandable some key points, namely:

- Time;
- Money;
- Support.

There are weaknesses on the results of this thesis. The most participated questionnaire had 84 replies and the bibliography found about this subject is scarce. Although this is a fact, I trust this results represent new data about the subject and constitute the basis for a fundamental reform that happening would help improve the quality of health care in Portugal and, at the same time, represent more money for Portuguese economy.

6. Conclusion / Recommendations

The return of the doctor-scientist must be a priority in order to ensure Portugal has better health care and a stronger economy. To improve Clinical Trials in Portuguese Family Medicine the Government of Portugal must provide time, money and support. Below there are twenty recommendations divided by this three very well defined areas for development.

6.1 To Provide Time

- To allow protected time for research to staff members;
- To delegate some routine family doctor's functions to other health professionals in order to gain doctor's time for research and therefore, not compromising the number of patient visits (especially bureaucracy);
- To encourage a sizeable number of Family Doctors into a parallel academic career, permitting investment of time in the academic area without losing salary money (e.g., 7-8/10 of the week schedule dedicated to the academic area and 2-3/10 of the week schedule dedicated to clinical work). Family Doctors should not be punished economically because of an academic career.

6.2 To Finance

- To professionalize researchers, economically rewarding them for research work – an additional specific payment, on top of the salary, for Family Doctors who work on Clinical Trials; Funding and a salary for research is fundamental. This is an opportunity for extra compensation for poorly paid but highly qualified professionals without sacrificing patients' time (e.g. working after hours on research);
- To reward research work when assessing health units; e.g. in a model B USF, research can be put as value indicator, bringing more money and resources to the unit;

- To increase the number of grants available from private and public nature. Direct financing for research in primary care must be a priority. Health Units should also be able to get direct financing for research from the Health Services Management;
- To easily allocate industry and grant funds to specific units that effectively do research, instead of to the central/regional administration. This money could even be used to increase the quality of support rooms for research, obtain better or even newer equipment, furniture, and refurnishing walls, computers without sacrificing the available budget;
- To facilitate industry promoted clinical trials. These will be important at least in the beginning; As soon as critical mass of researchers and know-how emerges, investigator (academic) research will become natural and will have its own funding also.

6.3 To Support

- To increase Family Doctors education for clinical research; trainees who want to be researchers must be adequately trained. The specialists must have the possibility of doing workshops and other specific courses, namely in Good Clinical Practice, pragmatic Research Design, Methodology, and Medical Statistics. This could be done by creating and developing a National Institute of Family Medicine aiming at specific training of Family Doctors, CME / CPD and research. It should be closely associated with Academic Departments of Family Medicine. A certain degree of separation and independence from the ministry of health is desired so that is better accepted by the Portuguese Family Doctors; Partnerships must be established between clinical units (with its research departments), education institutions and research institutions;
- To improve the infra-structures for research within Family Medicine Units; specifically rooms for trial master files or for subject assessment;
- To professionalize ethics committees and regulators specifically targeted for the need of Family Medicine research. This would improve timings for approval of Clinical Trials, by Ethics Committees and CNPD;
- To attract CROs and foundations for research in Family Medicine. Strategic and population aim of scientific knowledge must be valued because even if it is less pompous in its aims than basic research, generally does more to improve the health of citizens immediately and profoundly;

- To develop a structure at each ARS to deal with Promoters about all issues related with Clinical Trials. To simplify the communication and administrative process with the ACES, ARS and the regulators in order to promote faster approval for Clinical Trials. In fact, each ACES should have its research office to give support on a local basis;
- To establish and develop protocols for Clinical Trials. Standard procedures must be in place to receive Clinical Trials promoted by the Pharmaceutical Industry, through the creation of cooperation and partnership protocols between the Regional Health Administrations, Pharmaceutical Companies and CROs, encouraging activities which provide gains in training and clinical excellence for the professionals;
- To create regional and national Research Networks and integrate international Research Networks. Networks could even be divided by thematic classes like respiratory diseases, arterial hypertension, depression, diabetes and musculoskeletal diseases;
- To create a network for scientific literature access;
- To place Clinical Research and particularly Clinical Trials in the political agenda. In order to make Portugal assert itself as a valid player in the Clinical Research context, politics have the key role to change the current state of Portuguese clinical trials, taking advantage of an intellectual elite clearly capable of more and currently underused;
- To define a research agenda, choosing strategic therapeutic areas to focus in the near future, possibly choosing pragmatic Clinical Trials adequate to the reality of Family Medicine and to the needs in Health, in particular effectiveness of the interventions in Health and the national health plan;
- To contract support staff (statisticians, nurses, administrative, etc.) specifically for research. To choose one or more members of the practice teams to be in charge of promoting and managing research that should involve the whole team;
- To value research activity in the medical career. It is fundamental to review the medical career in order to give more emphasis to research work, recognizing the medical work as an investigator (Medicine is also research.) It must be given relevance to research in CME/CPD schemes.

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8. Attachments

8.1. Attachment 1 – “Portuguese GPs and the Clinical Trials Questionnaire – 2012”



Portuguese GPs and the Clinical Trials

QUESTIONNAIRE

This questionnaire is related to a Master of Science thesis by Manuel Pedro dos Santos Rodrigues Pereira and it has the objective of characterize how Portuguese GPs feel about Clinical Trials.

Please, complete data on gender, age and if you're a trainee or a specialist.

Gender:

Age:

Trainee/Specialist:

Below, there are some questions to be answered with a simple “yes/no”.

1. Did you ever have an interest in conducting clinical trials?
2. Are you aware of the regulatory requirements to conduct a clinical trial?
3. Do you know how to deal with the experimental drug during a trial?

4. Do you know what documents to submit to seek clinical trial approval?
5. Do you know what good clinical (for research) practices are?
6. Do you know the main rules and regulation to abide by during a clinical trial?
7. Do you know what requirements you must fulfil to close a clinical trial?
8. Do you know where to go to educate yourself about such requirements?
9. Does your health centre have infrastructures for conducting clinical trials?
10. Would an academic career in clinical trials fulfil your role as a GP?
11. Do you think that country can benefit from clinical trials?
12. Do you think the health system can benefit from clinical trials?

Do you agree with the following obstacles for clinical research (yes/no)?

- pressure to see the maximum number of patients
- lack of support personnel
- lack of financial initiatives
- no clear rules for compensation of the time invested in research
- the bureaucracy dealing with Infarmed, CEIC or CNPD (Comissão Nacional de Protecção de Dados) - too overwhelming for the time available to physicians, especially for those outside Lisbon who cannot deal directly with the regulatory managers at Infarmed, CEIC or CNPD.
- Once a MD becomes a specialist in family medicine, he no longer has flexibility to manage is non-clinical work.

Any other obstacle that is important to you:

Do you agree with the following recommendations to improve clinical research in Portugal (yes/no)?

- To put Clinical Research and particularly Clinical Trials in the political agenda
- To establish a system of effective communication between clinical units and GP academic departments.

- To delegate some routine family physician functions to other health professionals in order to gain physician's space and time for research and therefore not compromising the number of patient visits;
- To contracting support staff (statisticians, nurses, administrative, etc.) specifically for research;
- To improve cooperation between clinical units and family medicine university departments;
- To involve health care units in education and research networks;
- To give economical independence to health centres;
- To finance the practicing clinicians in order to conduct research; having protected time and being paid to work on studies.
- To obtain industry funds in a non-binding way to increase funds and support rooms, better equipment, even newer equipment, furniture, refurnishing walls, computers without sacrificing the available budget.

Any other suggestions to improve clinical trials in a primary care setting?

Thank you very much.

Until November 10th, 2012, please send back to: manuel_rodrigues_pereira@yahoo.co.uk

8.2 Attachment 2 – “Doing Clinical Trials in the Portuguese Family Medicine Context”



Doing Clinical Trials in the Portuguese Family Medicine Context

This questionnaire is related to a Master of Science thesis by Manuel Pedro dos Santos Rodrigues Pereira and it is intended to characterize how Portuguese GPs who ALREADY did Clinical Trials feel about it.

Please complete the following data:

Gender:

Age:

Trainee/Specialist:

Unit where the Clinical Trial was done:

Sponsor (Pharmaceutical Industry/Investigator Initiative):

Below, there are some questions to be answered:

- Three major obstacles:
- Three strategies to overcome the obstacles:
- Would you like to do get involved in another Clinical Trial (yes/no)?

Thank you very much.

Until November 10th, 2012, please send back to: manuel_rodrigues_pereira@yahoo.co.uk

8.3 Attachment 3 – “Clinical Trials and The Portuguese GPs Questionnaire – 2014”

This questionnaire is related to a Master of Science thesis by Manuel Pedro dos Santos Rodrigues Pereira and it has the objective of characterize how Portuguese GPs/Family Doctors (including trainees) feel about Clinical Trials.

Using a number from 0 to 20, answer the following questions:

- 1. In a weekly work schedule of 40 hours, how many would you like to have just to work on Clinical Trials?**
- 2. Classify the importance that Clinical Trials should have in the daily work of a Family Doctor.**
- 3. Classify how much do you agree with the use of scientific paper publication as criteria in the assessment of the Family Doctors.**
- 4. For the assessment of the Health Centre where you work, how much would you agree to have Clinical Trials development as a criteria?**
- 5. If you had the support from the leaders of the Portuguese National Health Service and also a suitable structure, with how much motivation would you work on Clinical Trials?**

Thank you very much.

Manuel Rodrigues Pereira

8.4 Attachment 4 – “Improving Clinical Trials in Portuguese Family Medicine” - The Vision of 15 Key Opinion Leaders

The following question is related to a Master of Science thesis by Manuel Pedro dos Santos Rodrigues Pereira and it has the objective of finding solutions to improve the development of Clinical Trials in the Portuguese Family Medicine.

It is very likely to quote your answer in the thesis, so by answering it, you understand that you are also authorizing the use of your answer associated to your name.

- **List 3 ideas that should be implemented in order to improve the development of Clinical Trials in the Portuguese Family Medicine.**

Thank you.

Manuel Rodrigues Pereira